

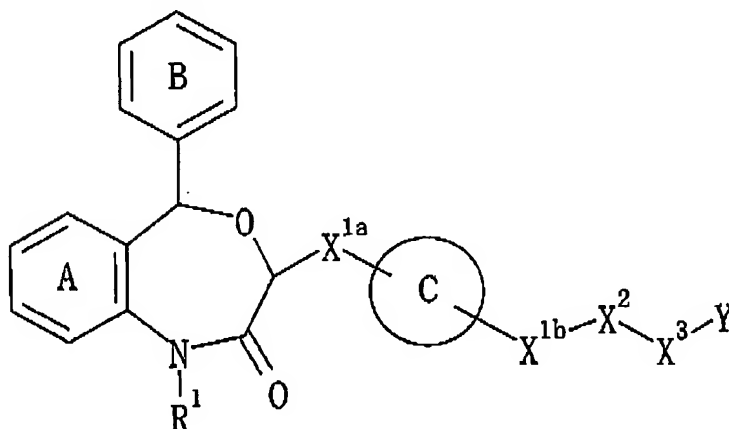
Application No.: 10/566,883  
Amendment dated August 20, 2009

Docket No.: 64788(70820)

### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently amended) A compound represented by the formula [1]:



wherein ring A and ring B each represent an optionally-substituted a benzene ring which may have 1 to 3 substituents selected from the group consisting of halogen, a C<sub>1-4</sub> alkyl group optionally substituted with halogen, a C<sub>1-4</sub> alkoxy group optionally substituted with halogen, a hydroxyl group, a nitro group, or a cyano group, or the adjacent substituents of said substituents may be taken together to form a ring,

ring C represents a benzene ring or a 5- to 6-membered monocyclic aromatic ring comprising at least 1 to 3 heteroatoms selected from oxygen, sulfur and nitrogen,

wherein the aromatic ring may be substituted with 1 to 4 substituents selected from the group consisting of (i) a carboxyl group optionally esterified with an optionally halogenated C<sub>1-4</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (ii) a phosphoric acid group optionally mono- or di-substituted with optionally halogenated C<sub>1-6</sub> alkyl or C<sub>2-7</sub> alkanoyloxy-C<sub>1-6</sub> alkyl, (iii) a sulfonic acid group, (iv) a sulfonamide group optionally substituted with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (v) a hydroxyl group or a sulfhydryl group, which may be optionally substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (vi) a carbamoyl group, (vii) a phenyl group optionally substituted with 1 to 5 substituents selected from the group consisting of hydroxyl, chlorine, fluorine, aminosulfonyl group, amino group optionally substituted with C<sub>1-3</sub> alkyl group and

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optionally bound to the aromatic ring via O or S, (viii) an amino group optionally mono- or di-substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (ix) a cyclic amino group optionally substituted with 1 to 3 C<sub>1-3</sub> alkyl, benzyl, or phenyl, (x) a 5- to 6-membered aromatic heterocyclic group containing 1 to 4 heteroatoms selected from N, O and S and optionally bound to the aromatic ring via O or S, (xi) a halogen atom, (xii) a C<sub>1-4</sub> alkyl group, a C<sub>1-4</sub> alkoxy group or a C<sub>1-4</sub> alkylthio group, each of which may be optionally substituted with a substituent selected from a halogen atom, a C<sub>1-4</sub> alkoxy group, a C<sub>1-4</sub> alkylthio group, carboxyl, and phenyl, (xiii) a C<sub>5-7</sub> cycloalkyl group, and (xiv) optionally halogenated C<sub>1-7</sub> alkanoyloxy, two of such substituents may be taken together to form C<sub>3-6</sub> alkylene, C<sub>3-6</sub> alkyleneoxy, or C<sub>3-6</sub> alkylenedioxy;

~~an optionally further substituted aromatic ring;~~

R<sup>1</sup> represents a C<sub>1-6</sub> alkyl group optionally substituted with 1 to 3 hydroxyl groups optionally substituted with C<sub>2-20</sub> alkanoyl or C<sub>1-7</sub> alkyl; lower alkyl group optionally substituted with an optionally substituted hydroxyl group;

X<sup>1a</sup> represents a bond or a C<sub>1-6</sub> alkylene optionally substituted with (i) a carboxyl group optionally esterified with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (ii) a phosphoric acid group optionally mono- or di-substituted with optionally halogenated C<sub>1-6</sub> alkyl or C<sub>2-7</sub> alkanoyloxy-C<sub>1-6</sub> alkyl, (iii) a sulfonic acid group, (iv) a sulfonamide group optionally substituted with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (v) a hydroxyl group or a sulfhydryl group, which may be optionally substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (vi) a carbamoyl group, (vii) a phenyl group optionally substituted with 1 to 5 substituents selected from the group consisting of hydroxyl, chlorine, fluorine, aminosulfonyl group, amino group optionally substituted with C<sub>1-3</sub> alkyl group and optionally bound to the aromatic ring via O or S, (viii) an amino group optionally mono- or di-substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (ix) a cyclic amino group optionally substituted with 1 to 3 C<sub>1-3</sub> alkyl, benzyl, or phenyl, (x) a 5- to 6-membered aromatic heterocyclic group containing 1 to 4 heteroatoms selected from N, O and S and optionally bound to the aromatic ring via O or S, (xi) a halogen atom, (xii) a C<sub>1-4</sub> alkyl group, a C<sub>1-4</sub> alkoxy group or a C<sub>1-4</sub> alkylthio group, each of which may be optionally substituted with a substituent selected from a halogen atom, a C<sub>1-4</sub> alkoxy group, a C<sub>1-4</sub> alkylthio group, carboxyl, and phenyl, (xiii) a C<sub>5-7</sub> cycloalkyl group, and (xiv) optionally halogenated C<sub>1-7</sub> alkanoyloxy, two of such substituents may be taken together to form C<sub>3-6</sub>

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alkylene, C<sub>3-6</sub> alkyleneoxy, or C<sub>3-6</sub> alkylenedioxy; or an oxo group; optionally-substituted lower alkylene,

X<sup>1b</sup> represents a bond or a C<sub>1-6</sub> alkylene optionally substituted with (i) a carboxyl group optionally esterified with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (ii) a phosphoric acid group optionally mono- or di-substituted with optionally halogenated C<sub>1-6</sub> alkyl or C<sub>2-7</sub> alkanoyloxy-C<sub>1-6</sub> alkyl, (iii) a sulfonic acid group, (iv) a sulfonamide group optionally substituted with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (v) a hydroxyl group or a sulfhydryl group, which may be optionally substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (vi) a carbamoyl group, (vii) a phenyl group optionally substituted with 1 to 5 substituents selected from the group consisting of hydroxyl, chlorine, fluorine, aminosulfonyl group, amino group optionally substituted with C<sub>1-3</sub> alkyl group and optionally bound to the aromatic ring via O or S, (viii) an amino group optionally mono- or di-substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (ix) a cyclic amino group optionally substituted with 1 to 3 C<sub>1-3</sub> alkyl, benzyl, or phenyl, (x) a 5- to 6-membered aromatic heterocyclic group containing 1 to 4 heteroatoms selected from N, O and S and optionally bound to the aromatic ring via O or S, (xi) a halogen atom, (xii) a C<sub>1-4</sub> alkyl group, a C<sub>1-4</sub> alkoxy group or a C<sub>1-4</sub> alkylthio group, each of which may be optionally substituted with a substituent selected from a halogen atom, a C<sub>1-4</sub> alkoxy group, a C<sub>1-4</sub> alkylthio group, carboxyl, and phenyl, (xiii) a C<sub>5-7</sub> cycloalkyl group, and (xiv) optionally halogenated C<sub>1-7</sub> alkanoyloxy, two of such substituents may be taken together to form C<sub>3-6</sub> alkylene, C<sub>3-6</sub> alkyleneoxy, or C<sub>3-6</sub> alkylenedioxy; or an oxo group; optionally-substituted lower alkylene;

X<sup>2</sup> represents a bond, -O- or -S-,

X<sup>3</sup> represents a bond or a divalent hydrocarbon group selected from the group consisting of (1) a C<sub>1-7</sub> straight or branched chain alkyl group, (2) a straight or branched chain C<sub>2-6</sub> alkenyl group, (3) a phenylene group, and (4) a divalent group in which phenylene and alkylene and/or alkenylene are combined; an optionally-substituted divalent hydrocarbon group, and

Y represents an optionally esterified or amidated carboxyl group selected from the group consisting of a carboxyl group, a C<sub>2-7</sub> alkoxy carbonyl group, a C<sub>7-14</sub> aryloxy carbonyl group, a C<sub>8-12</sub> aralkyloxy carbonyl group, a carbamoyl group, a N-C<sub>1-6</sub> alkyl carbamoyl group, a N,N-di-C<sub>1-6</sub> alkyl carbamoyl group, a N-C<sub>8-12</sub> aralkyl carbamoyl group, a N,N-di-C<sub>8-12</sub> aralkyl carbamoyl

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group, a 1-pyrrolidinylcarbonyl group, a piperidinocarbonyl group, and a morpholinocarbonyl group, or a salt thereof.

2. (Currently amended) The compound according to claim 1, wherein  $X^{1b}$  is a bond and Y is an optionally esterified carboxyl group selected from a carboxyl group, a  $C_{2-7}$  alkoxy carbonyl group, a  $C_{7-14}$  aryloxy carbonyl group, a  $C_{8-12}$  aralkyloxy carbonyl group, and a carbamoyl group.

3. (Original) The compound according to claim 1, wherein ring A is a benzene ring substituted with halogen atom(s).

4. (Currently amended) The compound according to claim 1, wherein ring B is a benzene ring substituted with ~~lower~~  $C_{1-4}$  alkoxy group(s).

5. (Currently amended) The compound according to claim 1, wherein ring C is an optionally ~~further~~ substituted monocyclic aromatic heterocyclic ring.

6. (Currently amended) The compound according to claim 1, wherein ring C is an optionally ~~further~~ substituted benzene ring.

7. (Original) The compound according to claim 1, wherein ring C is an optionally further substituted aromatic ring having no hydrogen atom that may be deprotonated.

8. (Original) The compound according to claim 1, wherein  $X^{1a}$  is  $C_{1-3}$  alkylene.

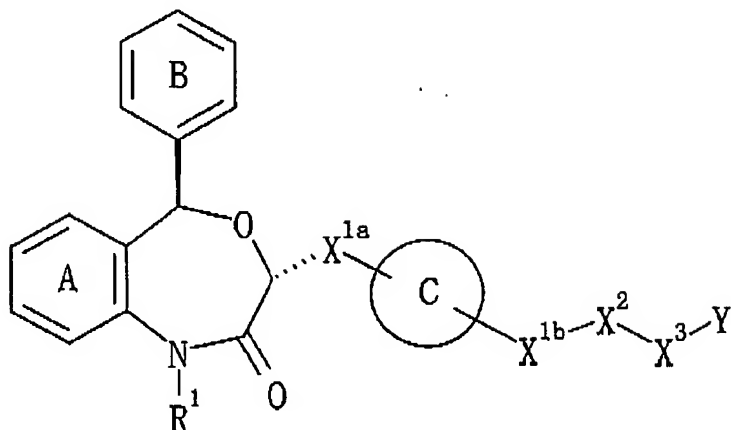
9. (Original) The compound according to claim 1, wherein  $X^2$  is a bond.

10. (Original) The compound according to claim 1, wherein  $X^3$  is  $C_{1-4}$  alkylene.

11. (Original) The compound according to claim 1, wherein the formula [I] is the formula [Ia]:

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wherein respective symbols are as defined in claim 1.

12. (Original) 3-(2-{3-[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]propyl}-1,3-thiazol-5-yl)propionic acid, 3-(2-{2-[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]ethyl}-1,3-thiazol-4-yl)propionic acid, or a salt thereof.

13. (Previously presented) 3-(2-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)propionic acid, 2-(2-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-isobutyl-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,3-oxazol-5-yl)acetic acid, or a salt thereof.

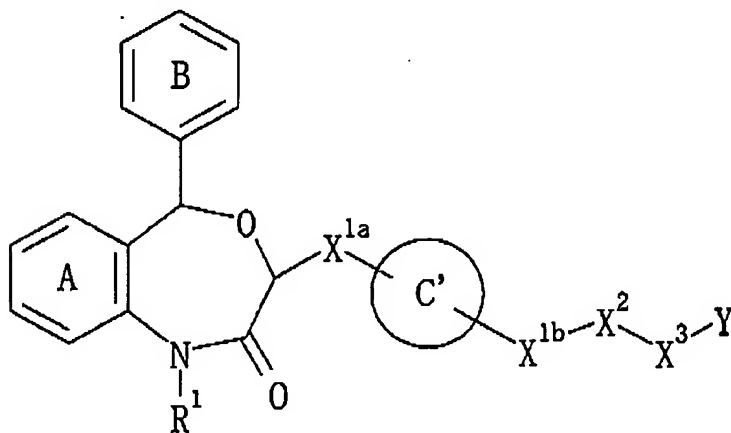
14. (Original) 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxadiazol-5-yl)pentanoic acid, 5-(3-{[(3R,5S)-7-chloro-5-(2,3-dimethoxyphenyl)-1-(3-hydroxy-2,2-dimethylpropyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxadiazol-5-yl)pentanoic acid, 5-(3-{[(3R,5S)-1-(3-acetoxy-2,2-dimethylpropyl)-7-chloro-5-(2,3-dimethoxyphenyl)-2-oxo-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-yl]methyl}-1,2,4-oxadiazol-5-yl)pentanoic acid, or a salt thereof.

15. (Canceled)

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16. (Currently amended) A medicine comprising the compound according to claim 1 ~~or a~~  
~~prodrug thereof~~.
17. (Currently amended) A medicine comprising a combination of the compound according  
to claim 1 ~~or a prodrug thereof~~ and a cholesterol lowering agent.
18. (Original) The medicine according to claim 16 or 17, which is a squalene synthase  
inhibitor.
19. (Original) The medicine according to claim 16 or 17, which is a triglyceride lowering  
agent.
20. (Original) The medicine according to claim 16 or 17, which is a lipid lowering agent.
21. (Original) The medicine according to claim 16 or 17, which is an agent for preventing or  
treating hyperlipemia.
22. (Original) The medicine according to claim 16 or 17, which is a high density lipoprotein-  
cholesterol level elevating agent.
23. (Currently amended) A process for preparing a compound represented by the formula  
[I']:



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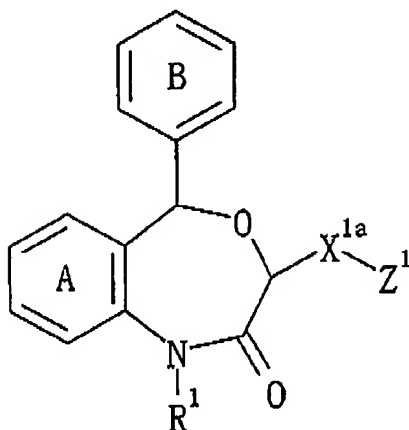
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wherein ring C' represents a benzene ring or a 5- to 6-membered monocyclic aromatic ring comprising at least 1 to 3 heteroatoms selected from oxygen, sulfur and nitrogen, wherein the aromatic ring may be substituted with 1 to 4 substituents selected from the group consisting of (i) a carboxyl group optionally esterified with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (ii) a phosphoric acid group optionally mono- or di-substituted with optionally halogenated C<sub>1-6</sub> alkyl or C<sub>2-7</sub> alkanovloxy-C<sub>1-6</sub> alkyl, (iii) a sulfonic acid group, (iv) a sulfonamide group optionally substituted with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (v) a hydroxyl group or a sulfhydryl group, which may be optionally substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (vi) a carbamoyl group, (vii) a phenyl group optionally substituted with 1 to 5 substituents selected from the group consisting of hydroxyl, chlorine, fluorine, aminosulfonyl group, amino group optionally substituted with C<sub>1-3</sub> alkyl group and optionally bound to the aromatic ring via O or S, (viii) an amino group optionally mono- or di-substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (ix) a cyclic amino group optionally substituted with 1 to 3 C<sub>1-3</sub> alkyl, benzyl, or phenyl, (x) a 5- to 6-membered aromatic heterocyclic group containing 1 to 4 heteroatoms selected from N, O and S and optionally bound to the aromatic ring via O or S, (xi) a halogen atom, (xii) a C<sub>1-4</sub> alkyl group, a C<sub>1-4</sub> alkoxy group or a C<sub>1-4</sub> alkylthio group, each of which may be optionally substituted with a substituent selected from a halogen atom, a C<sub>1-4</sub> alkoxy group, a C<sub>1-4</sub> alkylthio group, caroxyl, and phenyl, (xiii) a C<sub>3-7</sub> cycloalkyl group, and (xiv) optionally halogenated C<sub>1-7</sub> alkanovloxy, two of such substituents may be taken together to form C<sub>3-6</sub> alkylene, C<sub>3-6</sub> alkyleneoxy, or C<sub>3-6</sub> alkylenedioxy; an optionally further substituted aromatic heterocyclic ring and other symbols are as defined in claim 1, or a salt thereof, which comprises reacting a compound represented by the formula:

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wherein Z<sup>1</sup> represents a functional group involved in an aromatic heterocyclic ring forming reaction;

A and ring B each represent a benzene ring which may have 1 to 3 substituents selected from the group consisting of halogen, a C<sub>1-4</sub> alkyl group optionally substituted with halogen, a C<sub>1-4</sub> alkoxy group optionally substituted with halogen, a hydroxyl group, a nitro group, or a cyano group, or the adjacent substituents of said substituents may be taken together to form a ring.

R<sup>1</sup> represents a C<sub>1-6</sub> alkyl group optionally substituted with 1 to 3 hydroxyl groups optionally substituted with C<sub>2-20</sub> alkanoyl or C<sub>1-7</sub> alkyl;

X<sup>1a</sup> represents a bond or a C<sub>1-6</sub> alkylene optionally substituted with (i) a carboxyl group optionally esterified with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (ii) a phosphoric acid group optionally mono- or di-substituted with optionally halogenated C<sub>1-6</sub> alkyl or C<sub>2-7</sub> alkanoyloxy-C<sub>1-6</sub> alkyl, (iii) a sulfonic acid group, (iv) a sulfonamide group optionally substituted with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (v) a hydroxyl group or a sulfhydryl group, which may be optionally substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (vi) a carbamoyl group, (vii) a phenyl group optionally substituted with 1 to 5 substituents selected from the group consisting of hydroxyl, chlorine, fluorine, aminosulfonyl group, amino group optionally substituted with C<sub>1-3</sub> alkyl group and optionally bound to the aromatic ring via O or S, (viii) an amino group optionally mono- or di-substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (ix) a cyclic amino group optionally substituted with 1 to 3 C<sub>1-3</sub> alkyl, benzyl, or phenyl, (x) a 5- to 6-membered aromatic heterocyclic group containing 1 to 4 heteroatoms

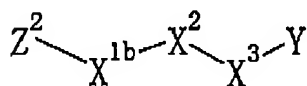


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selected from N, O and S and optionally bound to the aromatic ring via O or S, (xi) a halogen atom, (xii) a C<sub>1-4</sub> alkyl group, a C<sub>1-4</sub> alkoxy group or a C<sub>1-4</sub> alkylthio group, each of which may be optionally substituted with a substituent selected from a halogen atom, a C<sub>1-4</sub> alkoxy group, a C<sub>1-4</sub> alkylthio group, caroxyl, and phenyl, (xiii) a C<sub>5-7</sub> cycloalkyl group, and (xiv) optionally halogenated C<sub>1-7</sub> alkanoyloxy, two of such substituents may be taken together to form C<sub>3-6</sub> alkylene, C<sub>3-6</sub> alkyleneoxy, or C<sub>3-6</sub> alkylenedioxy; or an oxo group;  
and other symbols are as defined in claim 1, or a salt thereof,

with a compound represented by the formula:



wherein Z<sup>2</sup> represents a functional group involved in an aromatic heterocyclic ring forming reaction;

X<sup>1b</sup> represents a bond or a C<sub>1-6</sub> alkylene optionally substituted with (i) a carboxyl group optionally esterified with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (ii) a phosphoric acid group optionally mono- or di-substituted with optionally halogenated C<sub>1-6</sub> alkyl or C<sub>2-7</sub> alkanoyloxy-C<sub>1-6</sub> alkyl, (iii) a sulfonic acid group, (iv) a sulfonamide group optionally substituted with an optionally halogenated C<sub>1-6</sub> alkyl group or an optionally halogenated C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl group, (v) a hydroxyl group or a sulfhydryl group, which may be optionally substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (vi) a carbamoyl group, (vii) a phenyl group optionally substituted with 1 to 5 substituents selected from the group consisting of hydroxyl, chlorine, fluorine, aminosulfonyl group, amino group optionally substituted with C<sub>1-3</sub> alkyl group and optionally bound to the aromatic ring via O or S, (viii) an amino group optionally mono- or di-substituted with an optionally halogenated C<sub>1-3</sub> alkyl group, (ix) a cyclic amino group optionally substituted with 1 to 3 C<sub>1-3</sub> alkyl, benzyl, or phenyl, (x) a 5- to 6-membered aromatic heterocyclic group containing 1 to 4 heteroatoms selected from N, O and S and optionally bound to the aromatic ring via O or S, (xi) a halogen atom, (xii) a C<sub>1-4</sub> alkyl group, a C<sub>1-4</sub> alkoxy group or a C<sub>1-4</sub> alkylthio group, each of which may be optionally substituted with a substituent selected from a halogen atom, a C<sub>1-4</sub> alkoxy group, a C<sub>1-4</sub> alkylthio group, caroxyl, and phenyl, (xiii) a C<sub>5-7</sub> cycloalkyl group, and (xiv) optionally halogenated C<sub>1-7</sub> alkanoyloxy, two of such substituents may be taken together to form C<sub>3-6</sub> alkylene, C<sub>3-6</sub> alkyleneoxy, or C<sub>3-6</sub> alkylenedioxy; or an oxo group;

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X<sup>2</sup> represents a bond, -O- or -S-,

X<sup>3</sup> represents a bond or a divalent hydrocarbon group selected from the group consisting of (1) a C1-7 straight or branched chain alkyl group, (2) a straight or branched chain C2-6 alkenyl group, (3) a phenylene group, and (4) a divalent group in which phenylene and alkylene and/or alkenylene are combined; and

Y represents an optionally esterified or amidated carboxyl group selected from the group consisting of a carboxyl group, a C<sub>2-7</sub> alkoxycarbonyl group, a C<sub>7-14</sub> aryloxy carbonyl group, a C<sub>8-12</sub> aralkyloxy carbonyl group, a carbamoyl group, a N-C<sub>1-6</sub> alkylcarbamoyl group, a N,N-di-C<sub>1-6</sub> alkylcarbamoyl group, a N-C<sub>8-12</sub> aralkylcarbamoyl group, a N,N-di-C<sub>8-12</sub> aralkylcarbamoyl group, a 1-pyrrolidinyl carbonyl group, a piperidinocarbonyl group, and a morpholinocarbonyl group, and other symbols are as defined in claim 1, or a salt thereof.

24. (Currently amended) A method of inhibiting squalene synthase in a mammal, which comprises administering an effective amount of the compound according to claim 1 ~~or a prodrug thereof~~ to said mammal.

25. (Currently amended) A method of lowering triglyceride level in a mammal, which comprises administering an effective amount of the compound according to claim 1 ~~or a prodrug thereof~~ to said mammal.

26. (Currently amended) A method of lowering lipid level in a mammal, which comprises administering an effective amount of the compound according to claim 1 ~~or a prodrug thereof~~ to said mammal.

27. (Currently amended) A method of preventing or treating hyperlipemia in a mammal, which comprises administering an effective amount of the compound according to claim 1 ~~or a prodrug thereof~~ to said mammal.

28. (Currently amended) A method of elevating high density lipoprotein-cholesterol level in a mammal, which comprises administering an effective amount of the compound according to claim 1 ~~or a prodrug thereof~~ to said mammal.

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29-33. (Canceled)

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